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The Proportion and Associated Factors for Mortality among COVID-19 Infection with Diabetes in Iraq

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■ Abstract

Objective: The study aims to determine the proportion, clinical characteristics, and associated factors for the mortality among hospitalised COVID-19 patients with diabetes in Ramadi, Iraq. **Methods:** This retrospective cohort study included all adult diabetic patients with laboratory-confirmed COVID-19 who were hospitalised between January 2020 and December 2020 in Ramadi Province, Iraq. Data on demographics, medical history, and laboratory investigations were obtained from medical records. The poor outcomes were mortality during hospitalisation. Multivariate logistic regression was used to analyse for the associated factors for mortality. **Results:** A total of 545 health records of diabetic patients were reviewed. There were 340 males (62.4%) and 205 females (37.6%). The mean age was 64.54±10.86 years. The proportion of mortality was 32.84%. The protective factors for mortality were rural residency, duration of hospitalisation, and diabetic medication (SGLT inhibitors, DPP4 inhibitors and metformin). Cardiac disease, liver disease, temperature, CRP and D-dimer level were found to be predictive factors for mortality. **Conclusion:** The study revealed that the proportion of mortality among diabetic patients with COVID-19 infection was high in Iraq. The findings highlighted the predictive and protective factors among this vulnerable group for poor outcomes.

Keywords: COVID-19, DM, Diabetes, Mortality, ICU, Poor Outcomes.

1. Introduction

The coronavirus-2 (SARS-CoV-2) sometimes referred to as COVID-19 was made public in Wuhan, China, at the end of 2019. The primary complaint of this illness is Sever Acute Respiratory Syndrome (SARS). Globally, the illness spread quickly [1]. The WHO declared the epidemic to be a pandemic in March 2020 [2]. According to WHO data, the number of COVID-19-related deaths by October 2020 was close to 34.8 million [1]. The prevalence of diabetes mellitus (DM) among hospitalized COVID-19 patients varies by nation and by state within nations. The prevalence is influenced by a number of variables linked to COVID-19 and diabetes. According to Saha*et al.* [1], it was 9.7% in China and 28.3% in the US, and 35.5% in Italy [3]. The estimated prevalence of diabetes mellitus in patients with COVID-19 was 17% in five Asian nations [1].

Based on preliminary data released by the American Centers for Disease Control and Prevention on March 28, 2020, diabetes is the most prevalent underlying health condition among individuals infected with SARS-CoV-2, impacting roughly 10.9% of cases. Additionally, it is anticipated that diabetes patients made up 32% of all patients who needed to be admitted to the intensive care unit [4].

The weighted prevalence of mortality in hospitalized COVID-19 patients with DM is 20.0% with 95% confidence interval (CI): 15.0–26.0, according to data from 22 studies involving 45,775 COVID-19 patients. This is greater than the mortality rate in non-DM patients (11.0%, 95% confidence interval (CI): 5.0–16.0). Compared to the USA (20.0 %, 95% CI: 11.0-32.0) and Asia (17.0 %, 95% CI: 8.0-28.0), Europe had the highest prevalence of mortality among DM patients (28.0%; 95% CI: 14.0-44.0) [1].

Studies reveal an independent correlation between clinical and biological indicators such as age, micro- and macro-vascular complications of diabetes mellitus, dyspnea, and lowered platelet count with mortality risk among hospitalized COVID-19 patients with the disease [5].

Official data on particular death rates that provide insight into the number of deaths related to COVID-19-

related morbidities is lacking in Iraq. The purpose of this study is to identify mortality risk variables for COVID-19 patients in Iraq who have diabetes mellitus. The objective of this research is to ascertain the percentage, clinical features, and related variables of hospitalized COVID-19 patients with diabetes in Ramadi, Iraq.

2. Materials and Methods

Based on chart reviews, this study is retrospective in nature. In order to calculate the sample size, two proportions and two averages for the number of variables were compared in order to test the hypotheses regarding the proportions of death and ICU admission. Additionally, mean age and mean BMI hypotheses were put forth, and PS software version 3.1.2 was used to determine the maximum number of sample sizes.

Data were gathered by looking through the medical records of every person who visited the Al-Ramadi Teaching Hospital emergency room as a COVID-19 patient between January 1 and December 31, 2020. The inclusion and exclusion criteria were applied to these records in order to filter them. This form has a second CRF attached to it that was created specifically for data collecting. In light of this, 545 patient records were chosen, and their data was coded in unique Excel sheets before being moved to SPSS files for additional statistical analysis.

3. Results

A total of 545 case reports were reviewed and those with complete data were taken. The sample contained 205 (37.6%) female and 340 (62.4%) male. Type I DM patients were 49 (9%) of the selected sample, whereas type II DM patients were 496 (91%). Number of cases admitted to the ICU was 456 (83.7%). Mortality rate was 32.8%.

3.1. Simple and Multiple Logistic Regression for Associated Factors of Mortality in Diabetes Mellitus Patients with COVID-19 Infection

Ten factors from the univariable analysis were included in the multivariable analysis based on a p-value of less than 0.05. Ten factors from the univariable analysis were included in the multivariable analysis based on a p-value of less than 0.05. The multivariable analysis included the following variables: residency, length of hospital stay, white blood cells (WBC), medication for diabetes mellitus, cardiovascular illnesses, liver disease, fever, temperature, CRP, and D-dimer.

In the univariable analysis, there were six significant increased chances of mortality and four significant protective odds. However, the final model that fit the data only contained nine significant factors. In Table 1, simple and multiple logistic regression for mortality prediction factors in COVID-19 patients with diabetes mellitus are shown.

Table 1: Baseline Characteristic for the Mortality.

Variable	Mortality (n=179)	Survive (n=366)
Age (mean ± SD)	65.85 ± 10.57	63.89 ± 10.96
Duration (mean ± SD)	7.24 ± 3.20	12.63 ± 5.99
ICU admission n(%)	176 (38.6)	280 (61.4)
Mechanical ventilation n(%)	176 (44.8)	217 (55.2)
Gender n (%)		
Male	121 (35.6)	219 (64.4)
Female	58 (28.3)	147 (71.7)
Residential Area n (%)		
Urban	123 (44.4)	154 (55.6)
Rural	56 (20.9)	212 (79.1)
DM Type n (%)		
Type 1	29 (59.2)	20 (40.8)
Type 2	150 (30.2)	346 (69.8)
Medical History n (%)		
HPT	89 (35.3)	163 (64.7)
Cardiac disease	63 (52.5)	57 (47.5)
Kidney disease	41 (56.2)	32 (43.8)
Liver disease	72 (88.9)	9 (11.1)
Smoking n (%)	61 (38.4)	98 (61.6)
Disease Severity Variables n (%)		
Fever	167 (32.0)	355 (68.0)
Cough	179 (34.8)	336 (65.2)
Shortness of breath	179 (33.1)	362 (66.9)
Fatigue	179 (34.0)	348 (66.0)
Anorexia	179 (34.3)	343 (65.7)
Sputum production	159 (34.8)	298 (65.2)
Headache	179 (34.2)	344 (65.8)
Dehydration	179 (37.4)	299 (62.6)
Myalgia	179 (35.8)	321 (64.2)
Rinorrhea	120 (41.0)	173 (59.0)
Sorethroat	147 (37.8)	242 (62.2)
Vomit	57 (43.5)	74 (56.5)
Diarrhea	25 (27.8)	65 (72.2)
Nausea	174 (42.8)	233 (57.2)
Anosmia	94 (47.7)	103 (52.3)
Ageusia	111 (42.4)	151 (57.6)
Temperature(°C) (mean ± S.d.)	38.58 ± 0.480	38.12 ± 0.372
Respiratory rate (mean ± S.d.)	34.15 ± 4.47	28.83 ± 6.13
O2Sat (mean ± S.d.)	76.74 ± 15.45	82.42 ± 13.44
BMI (Kg/m^2) (mean ± S.d.)	22.60 ± 1.69	23.01 ± 1.48
Test for COVID-19 Status n (%)		
IgM (mg/L)	162 (32.4)	338 (67.6)

PCR	34 (29.8)	80 (70.2)
Radiological n (%)		
Chest X-ray: Bilateral peripheral consolidation	179 (33.2)	360 (66.8)
Chest CT scan: Peripheral ground-glass opacity	179 (33.5)	356 (66.5)
Medication n (%)		
DM		
Insulin	60 (54.5)	50 (45.5)
Metformin	30 (19.0)	128 (81.0)
Sulphonylureas	50 (31.4)	109 (68.6)
DPP4 inhibitors	5 (16.7)	25 (83.3)
SGLT inhibitors	34 (38.6)	54 (61.4)
HPT		
ARB	80 (31.1)	177 (68.9)
ACEi	0 (0.0)	27 (100.0)
Amlodipine	13 (38.2)	21 (61.8)
Statin	12 (52.2)	11 (47.8)
Antiplatelet	2 (15.4)	11 (84.6)
Anticoagulant	179 (36.0)	318 (64.0)
Investigations: Mean±S.d.		
WBC (thousand/μL)	12.10 ± 1.24	7.32 ± 0.73
CRP (mg/L)	5.14 ± 1.12	3.52 ± 2.04
D-dimer(mg/L)	1.69 ± 0.37	1.34 ± 0.31
LDH (U/L)	195.70 ± 7.52	195.58 ± 6.68
Ferritin (μg/L)	982.41 ± 341.93	679.06 ± 257.49
HbA1C (%)	12.48 ± 2.87	10.15 ± 2.56
FPG (mg/dL)	526.70 ± 142.91	471.88 ± 150.06
S. creatinine (mg/dL)	2.57 ± 1.65	2.19 ± 1.03
ALT (U/L)	22.83 ± 3.59	22.42 ± 3.08
AST (U/L)	24.80 ± 2.91	24.63 ± 3.30
Hb (g/dl)	12.83 ± 1.65	13.21 ± 1.83
Platelet (thousand/μL)	216.20 ± 94.88	216.55 ± 121.21

Table 2: Simple and Multiple Logistic Regression for Predictor Factors of Mortality in COVID-19 Patients with Diabetes Mellitus.

Variable	Simple Logistic Regression[a]			Multiple Logistic Regression[b]		
	Crude OR	(95% CI)	p-value	Adjusted OR	(95% CI)	p-value
Age (years)	1.017	(1.00,1.034)	<0.050	1.016	(0.981,1.053)	0.365
Residency (1)	0.33	(0.23, 0.48)	<0.001	0.052	(0.02, 0.141)	<0.001
Duration of hosp (days)	0.74	(0.69, 0.79)	<0.001	0.732	(0.658, 0.814)	<0.001
WBC (thousand/L)	17.46	(8.14, 37.43)	<0.001		Discarded	
DM Med			<0.001			<0.001
DM Med(1)	0.20	(0.11, 0.34)	<0.001	0.199	(0.055, 0.719)	0.014
DM Med(2)	0.38	(0.23, 0.63)	<0.001	0.500	(0.164, 1.525)	0.223
DM Med(3)	0.17	(0.06, 0.47)	0.001	0.006	(0.001, 0.060)	<0.001
DM Med [7] (4)	0.53	(0.30, 0.93)	0.027	0.007	(0.001, 0.041)	<0.001
Cardiac disease (1)	2.94	(1.94, 4.47)	<0.001	12.096	(2.265, 64.585)	0.001
Liver (1)	26.69	(12.92, 55.16)	<0.001	11.298	(3.847, 33.186)	<0.001
Fever (1)	0.43	(0.19, 0.99)	0.049	0.883	(0.242, 3.226)	0.851
Temperature	9.210	(5.942, 14.276)	<0.001	4.710	(2.023, 10.966)	<0.001
CRP (mg/L)	1.61	(1.44, 1.79)	<0.001	2.381	(1.804, 3.143)	<0.001
D-dimer (mg/L)	15.41	(8.69, 27.34)	0.000	7.103	(2.684, 18.798)	<0.001

[a]Simple logistic regression was applied
[b]Multiple logistic regression with backward Wald was applied.
Model fitness assessment: Hosmer-Lemeshow (X^2 =5.798, *p*-value = 0.670), classification table = 88.8%, Area under ROC curve = 0.964 (95%: 0.951, 0.977).

3.2. Interpretation

In Ramadi, Iraq, multiple logistic regression revealed that eight variables were statistically significant in predicting the death of COVID-19 patients who also had diabetes. Residency, length of hospital stay, and diabetic treatment were protective factors against death.

Compared to patients living in urban areas, those who lived in rural areas had a 5% lower chance of dying (adjusted OR= 0.05, 95% CI: 0.018, 0.134). Additionally, for every day that the length of hospitalization increased, there were 73.5% protective odds (adjusted OR= 0.735, 95% CI: 0.661, 0.817) against dying.

When compared to insulin, three diabetes medicines showed a substantial protective effect against death. When compared to insulin, SGLT inhibitors had the largest protective odds (adjusted OR= 0.007 (95% CI: 0.001, 0.040), followed by metformin (adjusted OR= 0.205 (95% CI: 0.056, 0.745) and DPP4 inhibitors (adjusted OR= 0.007 (95% CI: 0.002, 0.068).

Individuals with cardiac conditions are more likely than those without it to die from COVID-19 infection (adjusted OR=15.147, 95% CI: 3.019, 75.997). Individuals with liver disease are more likely than those without it to die from COVID-19 infection (12 (adjusted OR=12.0.35, 95% CI: 4.127, 35.098). It was discovered that D-dimer, CRP, and temperature were risk factors for the mortality status. A one-degree Celsius increase in temperature corresponds to a 4.633-fold increase in death risks. Likewise, an increase of one D-dimer and CRP unit indicates a 2.405 and 7.465 increase in mortality, respectively.

4. Discussion

According to this study, the mortality rate for COVID-19-positive diabetes patients was 32.84%. This death rate is significantly higher than what Saha (20%) discovered [1] and greater than what Saha (20%) discovered in Europe (28%), the USA (20%), and Asia (17%). Huang*et al.* [8] conducted a meta-analysis in which they found that the death rate ranged between being below and above the study's mortality rate. Miller*et al.* [9] investigation revealed that the combined death rate across several studies was 9.9%, with a range of 8.9–11.1% [9]. The quality of medical care, drugs, patients' state of health, and many other factors all affect the mortality rate. Consequently, the variation in the death rate shows the effectiveness of health policies overall.

Compared to other DM medications, metformin users have a decreased death risk [10]. While it may have contributed to the lower death rate when compared to other diabetes patients using different drugs, this outcome is consistent with our findings for this kind of medication. The effectiveness of a drug when combined with additional drugs for the same sample or when combined with samples from different studies. As such, it is not possible to generalize the results or propose them as a set of guidelines for future work.

Metformin users showed a lower death risk than non-users when it came to type 2 diabetes mellitus patients hospitalized with COVID-19 disease. Using metformin, whether on its own or in combination with other drugs, has been associated with a decreased risk of death. The largest benefit was seen by those taking a daily dose of ≥1000 mg to <2000 mg [10]. Another investigation on patients with type II diabetes mellitus infected with COVID-19 similarly confirmed this conclusion, indicating that the death rate among metformin users on day 28 of hospitalization was 16%, while it was 28.6% among non-users [10]. Our results are consistent with these observations. According to Izzi-Engbeaya*et al.* [11] metformin was observed to have an adverse effect on the first rates of death and ICU admission among diabetic patients during the first month of COVID-19. Despite the lack of conclusive evidence, metformin may serve as a protective factor against COVID-19 infection.

DPP-4 inhibitors have been shown in earlier studies to dramatically lower levels of important inflammatory cytokines, including interleukin-6 (IL-6), which directly affects COVID-19. Moreover, it has been shown that in cases of acute lung injury, pulmonary hyperinflammation is significantly reduced by DPP-4 inhibition. An applicable experimental model supports this, showing that sitagliptin reduced lipopolysaccharide-induced lung injury in mice via lowering the production of cytokines by human lung microvascular endothelial cells, such as TNF-α and IL-6 [12]. DPP-4 was shown to have no discernible impact on either the death rate or ICU admission in our study.

In the Northeast and Mid-Atlantic areas of the United States, metropolitan counties had the highest incidence rate of COVID-19 infections (3400 per 100000) compared to rural counties (1248 per 100000) [13]. Zhang*et al.* [14] conducted a study which revealed that the incidence and mortality rates of COVID-19 were not expected in certain rural and non-metropolitan counties. The discrepancy was explained by factors such as population density, poverty, and the proportion of elderly people. The use of a regression model revealed a positive correlation between the incidence rates and mortality rates. Rural locations were shown to be protective factors against the COVID-19 death rate in our study, which differs from Zhang and Schwartz's findings despite the fact that patients from rural areas had lower mortality and ICU admission rates than their urban counterparts. Furthermore, our research supported the findings of Cuadros*et al.* [13] that COVID-19 incidence is lower in rural than in urban settings.

In the past, residences in rural Iraq were largely situated within farms. Consequently, living in a rural region offers sufficient space between neighbors to mitigate the negative impacts of dense population that might arise in cities and towns, where there is a higher risk of infectious diseases. Because they are isolated from individuals who live in populated regions, residents of rural areas have a lower risk of catching diseases. They also used to consume their own dairy products, fruits, and vegetables.

On the contrast of our findings, Ramirez*et al.* [15], found that the highest fatality rates were belong to rural counties and that rural counties were at greater risk of death [15].

The escalation of patients' complaints and symptoms may be brought on by the hospital's inability to accept such patients, social customs that prevent people from disclosing their illnesses to others, a propensity for using conventional medications to treat their conditions, or a lack of awareness about their conditions. COVID-19.

Chen*et al.* [16] found that individuals with diabetes and COVID-19 had a greater frequency of hypertension, which is the principal comorbidity of the virus, compared to individuals with the infection but not diabetes. Although simple and complex logistic regression models did not identify hypertension as a significant factor linked with mortality, this result is consistent with the findings of our investigation.

Elevated blood glucose levels were found to be an independent risk factor for death among the COVID-19 participants in a cohort of studies using multivariable regression analysis. The sole independent risk factor for death or a poor prognosis in individuals with COVID-19 and diabetes was CRP, a novel infection-related biomarker that links inflammation and chronic diseases like diabetes in addition to identifying secondary infections [16] According to this study, CRP strongly affected mortality status.

Although it was not found to be a significant factor associated with mortality in this study, D-dimer is essentially higher in diabetic patients with COVID-19 [17], which may point out the virus effect on thrombopoiesis or platelets of survivors. In this context, D-dimer of our study was also essentially higher than normal limit (average = 1.45 with a standard deviation of 0.37).

5. Declaration

5.1 Acknowledgement

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5.2 Conflict of Interest

The authors declare that there is no conflict of interest

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